Association between serum vitamin D status and functional mobility in memory clinic patients aged 65 years and older

Gschwind, Yves J ; Bischoff-Ferrari, Heike A ; Bridenbaugh, Stephanie A ; Härdi, Irene ; Kressig, Reto W

Abstract: Background: Recent studies have shown that vitamin D status may be relevant for physical and cognitive performance in the older population. This association may be of particular interest to older people at risk for cognitive impairment and functional decline. Objective: The aim of this study was to determine the association between serum 25-hydroxyvitamin D [25(OH)D] status and functional mobility in seniors assessed in a memory clinic. Methods: We conducted a cross-sectional study of outpatients (n = 404) in a memory clinic. Functional mobility was assessed with three endpoints: normal and fast walking speed and the Timed Up and Go (TUG) test. Adjusted multivariate analyses in all patients and two pre-planned subgroup analyses in vulnerable seniors (previous fall and MMSE score of 26 or no previous fall and MMSE score of <26) versus less vulnerable seniors (no previous fall and MMSE score of 26) were performed to assess the association of 25(OH)D and functional mobility. Results: Overall, mean 25(OH)D serum levels were 63.2 ± 33.9 nmol/l, and 41.3% were vitamin D deficient (<50 nmol/l). Seniors in the lowest 25(OH)D quartile (<39 nmol/l) had significantly worse functional mobility compared to the highest 25(OH)D quartile (>81 nmol/l); adjusted for all covariates, seniors in the highest quartile performed 9.4% better in normal (p = 0.02) and 9.2% better in fast (p = 0.004) walking speed, and 4.4% better in the TUG test (p = 0.24). The association between 25(OH)D status and functional mobility was most pronounced in less vulnerable seniors (p for trend significant for all three mobility tests). Seniors with a higher 25(OH)D status also had better cognitive function (MMSE score; p = 0.006). Conclusions: Lower serum 25(OH)D status is associated with poorer functional mobility and cognitive function, therefore supporting 25(OH)D assessment in this population at risk for both functional and cognitive decline. © 2013 S. Karger AG, Basel.

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Association between Serum Vitamin D Status and Functional Mobility in Memory Clinic Patients Aged 65 Years and Older

Yves J. Gschwind[a] Heike A. Bischoff-Ferrari[c, d] Stephanie A. Bridenbaugh[a]
Irene Härdi[a] Reto W. Kressig[b]

[a]Basel Mobility Center, Department of Acute Geriatrics, University Hospital Basel, and [b]Department of Acute Geriatrics, Felix Platter Hospital and University of Basel, Basel, [c]Center on Aging and Mobility, University of Zurich and City Hospital Waid, and [d]Department of Geriatrics, University Hospital Zurich, Zurich, Switzerland

Key Words
Vitamin D · Physical function · Gait velocity · Fall prevention · Older adults

Abstract
Background: Recent studies have shown that vitamin D status may be relevant for physical and cognitive performance in the older population. This association may be of particular interest to older people at risk for cognitive impairment and functional decline. ***Objective:*** The aim of this study was to determine the association between serum 25-hydroxyvitamin D [25(OH)D] status and functional mobility in seniors assessed in a memory clinic. ***Methods:*** We conducted a cross-sectional study of outpatients (n = 404) in a memory clinic. Functional mobility was assessed with three endpoints: normal and fast walking speed and the Timed Up and Go (TUG) test. Adjusted multivariate analyses in all patients and two pre-planned subgroup analyses in vulnerable seniors (previous fall and MMSE score of ≥26 or no previous fall and MMSE score of <26) versus less vulnerable seniors (no previous fall and MMSE score of ≥26) were performed to assess the association of 25(OH)D and functional mobility. ***Results:*** Overall, mean 25(OH)D serum levels were 63.2 ± 33.9 nmol/l, and 41.3% were vitamin D deficient (<50 nmol/l). Seniors in the lowest 25(OH)D quartile (<39 nmol/l) had significantly worse functional mobility compared to the highest 25(OH)D quartile (>81 nmol/l); adjusted for all covariates, seniors in the highest quartile performed 9.4% better in normal (p = 0.02) and 9.2% better in fast (p = 0.004) walking speed, and 4.4% better in the TUG test (p = 0.24). The association between 25(OH)D status and functional mobility was most pronounced in less vulnerable seniors (p for trend significant for all three mobility tests). Seniors with a higher 25(OH)D status also had better cognitive function (MMSE score; p = 0.006). ***Conclusions:*** Lower serum 25(OH)D status is associated with poorer functional mobility and cognitive function, therefore supporting 25(OH)D assessment in this population at risk for both functional and cognitive decline.

Introduction

Traditionally, vitamin D has been linked to bone health [1], and vitamin D supplementation is supported as an evidence-based strategy in fracture risk reduction among adults aged 65 years and older [2, 3]. In a most recent pooled analysis of source data of 11 double-blind randomized controlled trials including 31,022 seniors, vitamin D supplementation at an actual median intake of 800 IU per day (range 792–2,000) reduced hip fracture

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Dr. phil. Yves J. Gschwind
Basel Mobility Center, University Hospital Basel
Schanzenstrasse 55
CH–4031 Basel (Switzerland)
E-Mail y_gschwind@bluewin.ch

risk by 30% [4]. However, there remains controversy about the optimal vitamin D serum level and dose for fracture prevention [5]. Mechanistically, the benefit for fracture prevention may be explained by the well-established positive effect of vitamin D on calcium absorption [6]. Alternatively, several lines of evidence support a direct effect of vitamin D on muscle [7, 8], and several meta-analyses on trials of vitamin D supplementation support vitamin D as an effective strategy in fall prevention [9, 10], as reflected in the American and British Geriatric Society Guidelines [11]. Moreover, vitamin D may act on the central nervous system influencing neurophysiologic function essential for motor control [12].

At the same time, the prevalence of vitamin D deficiency is reported to be 50% or more among large parts of the senior population worldwide [13–15]. Serum 25-hydroxyvitamin D [25(OH)D] represents the best clinical measure of systemic vitamin D status [16]. Seniors are at increased risk of vitamin D deficiency due to less time spent outside, use of sun protection, less dietary intake, and institutionalization [13, 17]. Furthermore, with age, the skin capacity to produce vitamin D from UVB exposure is reduced by a factor of 4 [18].

In the general senior population, vitamin D deficiency has been associated with reduced muscle strength and functional mobility [19, 20], as well as a higher risk of cognitive decline [21], which, in combination, may lead to an increased risk of falls, fractures [22–24], and nursing home admission [25]. In this large survey of seniors admitted to a memory clinic, we examined the association between vitamin D status and functional mobility. We hypothesized that serum 25(OH)D acts as a mediator of improved functional mobility and that there is an association between vitamin D and cognition in seniors assessed at a memory clinic. Further, we explored whether these associations differ between less vulnerable and vulnerable seniors.

Subjects and Methods

Study Population

Data from 579 consecutive memory clinic patients at risk for cognitive and functional decline assessed in an ambulatory setting between September 2008 and April 2011 were screened for eligibility. A total of 175 patients were excluded from the data analysis, because they fulfilled at least one of the following exclusion criteria: younger than 65 years of age, use of walking aid, or missing data [25(OH)D, normal or fast walking speed, age, gender, height, weight, Mini-Mental State Examination (MMSE) score, number of prescription drugs, or Timed Up and Go (TUG) results]. Data from the remaining 404 patients were analyzed for this study. This study was approved by the local ethics committee (Canton Basel, reference number EK 365/11).

The examination battery applied at the Memory Clinic of the University Hospital Basel included the MMSE (the maximum score is 30 points: 0–10 = severe cognitive impairment; 11–20 = moderate cognitive impairment; 21–26 = mild cognitive impairment, and 27–30 = normal cognitive function) as a measure of global cognitive function [26] and a functional mobility assessment (measurements of TUG and gait analysis) at the Basel Mobility Center. Further, a physical examination was performed by a physician, including recording of height and weight, the medical history, and the number of prescription drugs taken (self-report, report from caregivers, and/or documented medical history). We used the latter as a surrogate for comorbidity. In addition, the physician explored the history of falls in the previous 12 months, including observations by accompanying caregivers. A fall was defined according to the Prevention of Falls Network Europe (ProFaNE) as 'an unexpected event in which the participant comes to a rest on the ground, floor, or lower level' [27]. Further, blood was drawn by nurses at the Memory Clinic for the assessment of 25(OH)D status and other relevant biomarkers.

We defined less vulnerable and vulnerable individuals based on their cognitive performance in the MMSE and previous fall history (in the last 12 months) [28]. Less vulnerable seniors had no previous fall and a MMSE score of ≥26. Vulnerable seniors either had a previous fall and an MMSE score of ≥26 or had no previous fall and a MMSE score of <26.

Functional Mobility Assessment

For functional mobility, three tests were evaluated: normal and fast walking speed, and the TUG test. Patients wore their normal clothes, their own shoes, and a safety belt. The test administrator walked beside and slightly behind the patient to provide assistance and grab the safety belt if balance loss occurred while walking.

Normal and Fast Walking Speed

A 972 cm long electronic walkway with integrated pressure sensors (GAITRite® Gold and Platinum, CIR Systems, Sparta, N.J., USA) was used for gait analyses according to the European guidelines for clinical applications of spatiotemporal gait analysis in older adults [29]. Detailed testing procedures have previously been described by Bridenbaugh and Kressig [30]. Patients were verbally instructed regarding the gait analysis testing procedure: first, they had to walk at their usual speed (self-selected pace) and then as fast as possible (fast walking, but not running). No practice walks were performed before testing. Each walk was performed once.

Timed Up and Go Test

The TUG assesses basic mobility in seniors and was conducted at the Basel Mobility Center prior to the walking speed assessments [31]. When performing the TUG, the time in seconds that it takes an individual to rise from an armchair with armrests, walk 3 m at their regular walking speed, turn, walk back, and sit down again is measured using a stop watch.

Serum 25(OH)D Assay

Blood samples for the determination of 25(OH)D concentrations were obtained by a nurse from the Memory Clinic and analyzed at the Laboratory of Immunology at the University Hospi-

Table 1. Characteristics of memory clinic patients aged 65 years and older by vulnerability status and by quartile of 25(OH)D status

Characteristics	All (n = 404)	Less vulnerable patients (n = 322)	Vulnerable patients (n = 82)	p[a]	Serum 25(OH)D level quartile				p[b]
					1 <39 nmol/l (n = 101)	2 39–54 nmol/l (n = 97)	3 55–81 nmol/l (n = 105)	4 >81 nmol/l (n = 101)	
Serum 25(OH)D, nmol/l	63.2±33.9	65.3±34.4	55.1±30.8	0.02	29.8±6.1	46.2±4.9	66.2±7.4	109.9±30.1	<0.001
Age, years	77.6±5.8	77.1±5.8	79.1±5.4	0.005	78.9±5.6	78.0±5.8	76.2±5.8	77.2±5.5	0.005
BMI, kg/m^2	25.2±4.9	25.4±4.0	24.1±3.3	0.002	25.7±4.2	25.2±4.0	25.7±3.9	24.0±3.3	0.004
MMSE score	24.5±4.1	25.4±3.6	20.8±4.2	<0.001	23.4±4.4	24.4±4.2	24.6±4.0	25.4±3.8	0.006
Prescription drugs, n	3.7±2.6	3.9±2.7	3.7±2.6	0.594	3.7±2.7	3.6±2.5	3.9±2.8	4.1±2.7	0.46
TUG, s	12.1±3.3	11.8±3.0	13.3±4.0	0.002	12.9±3.2	12.0±3.3	11.8±3.2	11.8±3.2	0.06
Normal walking speed, cm/s	110.0±22.7	117.7±22.9	103.2±20.8	0.003	102.3±21.6	110.8±23.4	113.5±22.0	113.3±22.2	<0.001
Fast walking speed, cm/s	150.3±31.6	153.9±31.1	136.1±30.0	<0.001	137.3±27.8	151.9±32.9	155.3±31.5	156.6±30.6	<0.001

Data are means ± standard deviation. [a] Differences between groups were assessed using Student's t test. [b] Differences between 25(OH)D quartiles were assessed using analysis of variance.

tal Basel. An automated enzyme immune assay analyzer named DSX (Dynex Technologies, Chantilly, Va., USA) was used for 25(OH)D quantification in human serum. Samples were diluted with biotin-labeled 25(OH)D and incubated in microtiter wells. Enzyme-labeled avidin was added and bound selectively to complexed biotin followed by developing color using a chromogenic substrate. The absorbance of the stopped reaction mixtures was read in a microtiter plate reader, whereby the color intensity is inversely proportional to the concentration of 25(OH)D. The intra-assay and inter-assay coefficients of variation for 25(OH)D were 5.3 and 4.6%, respectively [32].

Statistical Analyses

The baseline characteristics of the 404 memory clinic patients were summarized using means and standard deviations or frequencies and percentages, as appropriate, in all, in less vulnerable (no previous fall and a MMSE score of ≥26) and vulnerable (previous fall and a MMSE score of ≥26 or no previous fall and a MMSE score of <26) seniors, and by quartile of 25(OH)D status. Serum 25(OH)D levels were assessed as quartiles (<39, 39–54, 55–81, and >81 nmol/l). General linear models were performed to evaluate differences in walking speed (normal and fast) and TUG by 25(OH)D quartile for all, less vulnerable and vulnerable seniors adjusted for age, gender, body mass index (BMI), MMSE, number of prescription drugs, and previous falls (yes/no). Analyses were conducted with SAS version 9.2 (SAS Institute, Cary, N.C., USA) software. All p values are two-sided.

Results

A total of 404 memory clinic patients (mean age 77.6 ± 5.8 years, 53.5% female) were included in this survey. Table 1 describes important covariates of the study population by vulnerability and quartile of 25(OH)D status. The overall mean MMSE score was 24.5 ± 4.1 points (range 5–30). Altogether, 37.4% (n = 151) of seniors took >5 prescription drugs, 28.2% (n = 114) took between 3 and 5, and 34.4% (n = 139) took <3.

25(OH)D Status

Mean 25(OH)D status was 63.2 ± 33.9 nmol/l; 4.7% (n = 19) had serum levels <25 nmol/l (severe deficiency), 41.3% (n = 134) had levels <50 nmol/l (deficiency), and 69.8% (n = 282) had levels <75 nmol/l (threshold for optimal fall and fracture reduction) [33]. Seniors with higher 25(OH)D status had a significantly higher MMSE score (p = 0.006).

Association between 25(OH)D Status and Functional Mobility in All Seniors

At the univariate level, seniors in the lowest 25(OH)D quartile (<39 nmol/l) had significantly worse functional mobility performance for all three functional mobility measures (normal and fast walking speed and TUG) when compared to the highest 25(OH)D quartile (>81 nmol/l). There was a pattern that suggested that all seniors in 25(OH)D quartile levels >39 nmol/l had an equally better function than those in the lowest quartile. This pattern was maintained for all functional mobility measures also in the multivariate analyses after adjustment for age, gender, BMI, MMSE, prescription drugs, and falls (fig. 1). We found no linear association between 25(OH)D and walking speed.

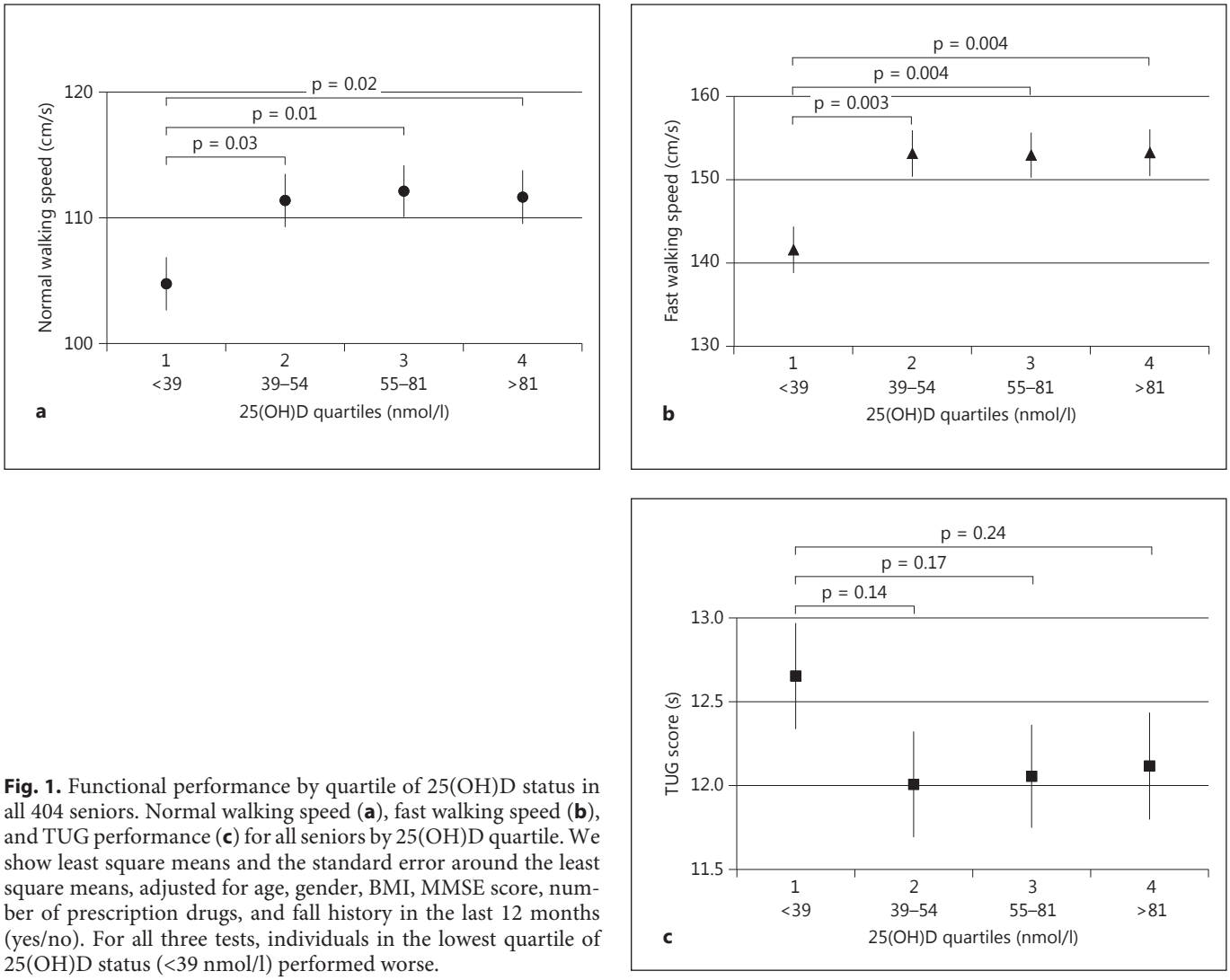

Fig. 1. Functional performance by quartile of 25(OH)D status in all 404 seniors. Normal walking speed (**a**), fast walking speed (**b**), and TUG performance (**c**) for all seniors by 25(OH)D quartile. We show least square means and the standard error around the least square means, adjusted for age, gender, BMI, MMSE score, number of prescription drugs, and fall history in the last 12 months (yes/no). For all three tests, individuals in the lowest quartile of 25(OH)D status (<39 nmol/l) performed worse.

Association between 25(OH)D Status and Functional Mobility in Less Vulnerable and Vulnerable Seniors

Compared to vulnerable seniors, less vulnerable seniors (no previous fall and MMSE ≥26) showed a more pronounced association between all three functional mobility measures and 25(OH)D quartile level. Notably, in the subgroup of less vulnerable seniors, the pattern of association changed from a threshold of 39 nmol/l as observed in the total study population to a trend for better performance with higher 25(OH)D status. In less vulnerable seniors, this trend was significant for normal and fast walking speed and TUG performance (fig. 2).

Discussion

In this large survey of 404 consecutive ambulatory memory clinic patients aged 65 years and older, low serum 25(OH)D status was not only associated with a lower MMSE score, but also with decreased functional mobility. Including both less vulnerable and vulnerable seniors as defined by their cognitive status and prior fall status, a 25(OH)D threshold of 39 nmol/l (upper end of the lowest quartile) was suggested for better functional mobility. However, in the subgroup of less vulnerable seniors (n = 322), there was a significant trend for better functional mobility (normal and fast walking speed and TUG) with a higher 25(OH)D quartile status, with a desirable threshold of >81 nmol/l for optimal functional mobility.

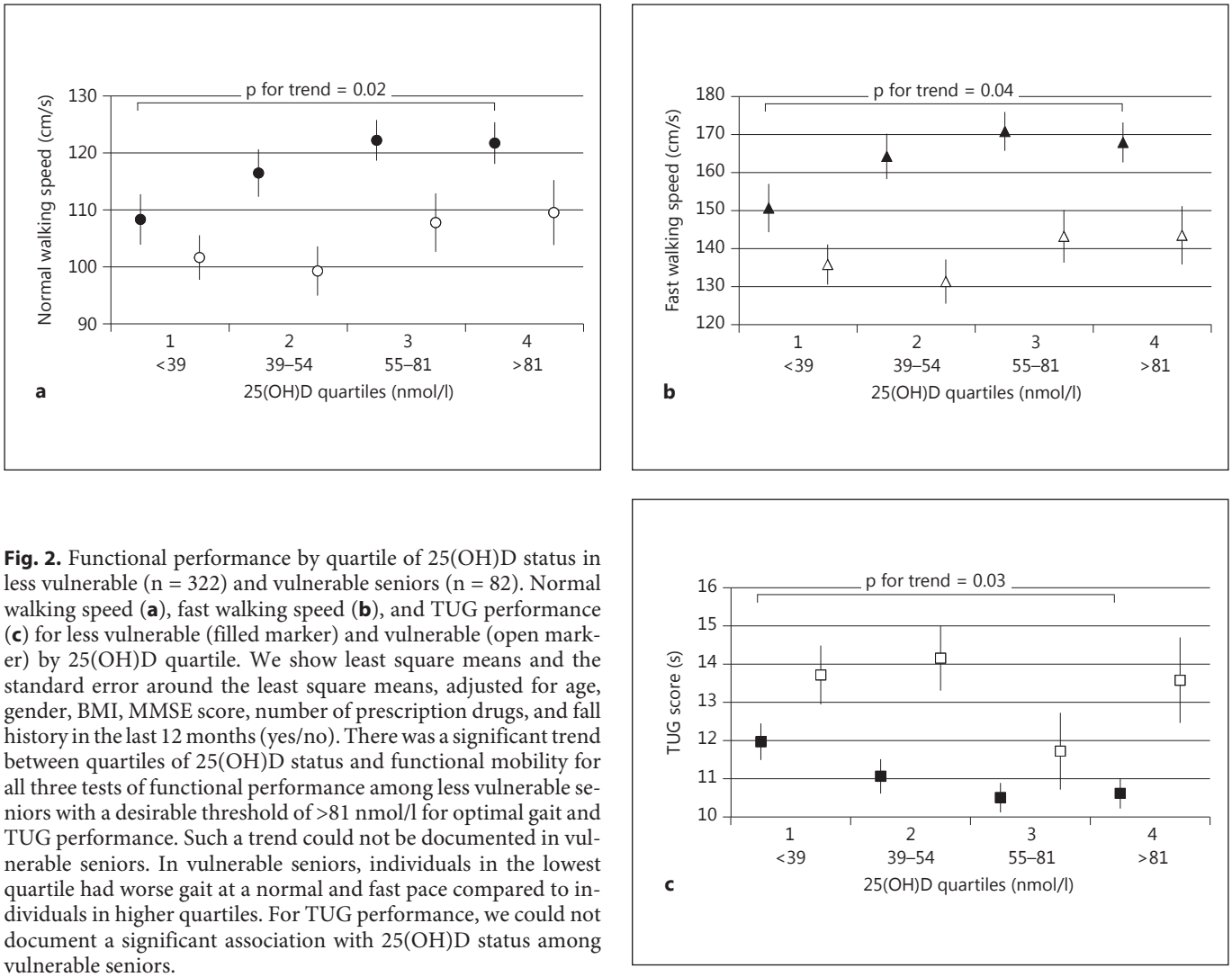

Fig. 2. Functional performance by quartile of 25(OH)D status in less vulnerable (n = 322) and vulnerable seniors (n = 82). Normal walking speed (**a**), fast walking speed (**b**), and TUG performance (**c**) for less vulnerable (filled marker) and vulnerable (open marker) by 25(OH)D quartile. We show least square means and the standard error around the least square means, adjusted for age, gender, BMI, MMSE score, number of prescription drugs, and fall history in the last 12 months (yes/no). There was a significant trend between quartiles of 25(OH)D status and functional mobility for all three tests of functional performance among less vulnerable seniors with a desirable threshold of >81 nmol/l for optimal gait and TUG performance. Such a trend could not be documented in vulnerable seniors. In vulnerable seniors, individuals in the lowest quartile had worse gait at a normal and fast pace compared to individuals in higher quartiles. For TUG performance, we could not document a significant association with 25(OH)D status among vulnerable seniors.

Vitamin D has been linked to cognitive performance in seniors [34]. In a retrospective study of older patients assessed in a memory clinic, 25(OH)D status was positively correlated with the MMSE [35]. Another recent study evaluated the effects of vitamin D supplementation on cognition in seniors referred to a memory clinic and reported a 25(OH)D-associated improvement in MMSE score [36]. Our study confirms these findings, documenting a significant association between a higher 25(OH)D level and better cognitive performance assessed with the MMSE in seniors examined at a memory clinic.

Several previous studies [37], including EPIDOS (Epidémiologie de l'Ostéoporose) [38], the Cardiovascular Health All Stars study [19], and the population-based NHANES III study [7], support an inverse association between higher 25(OH)D status and faster walking speed among community-dwelling seniors. The benefit of vitamin D supplementation (800–1,000 IU) on TUG performance was recently confirmed in a meta-analysis among seniors aged 60 years and older [39]. Our study extends to seniors assessed in a memory clinic, supporting at the cross-sectional level a positive association between higher 25(OH)D status and functional mobility, including TUG and gait performance.

In the present study, 41.3% of individuals were vitamin D deficient and 69.8% did not reach the desirable threshold of 75 nmol/l for fall and fracture prevention [33]. These data are consistent with international reports where about 50% of ambulatory seniors are expected to

have vitamin D deficiency [13, 14], and about 70% fall below a threshold of 75 nmol/l [4, 7].

As a surprise to the authors, less vulnerable seniors (no previous fall and MMSE ≥26) expressed a more linear association between 25(OH)D quartile status and gait and functional mobility with a desirable 25(OH)D threshold of >81 nmol/l for optimal performance. Comparing extreme quartiles in less vulnerable seniors, the threshold of >81 nmol/l was associated with an about 11% better performance in gait (normal and fast) and TUG compared to the lowest 25(OH)D quartile (<39 nmol/l). Our expectation was that vulnerable seniors may be more susceptible to 25(OH)D status. However, including these seniors, only the lowest quartile was associated with worse functional mobility compared to the other quartiles, suggesting a lower threshold of 39 nmol/l. This may be explained by an added level of impairment by a previous fall or reduced cognitive function, which may camouflage a positive association between 25(OH)D status and functional mobility.

Our study has several strengths. We measured 25(OH)D status, gait, and the TUG in a standardized way in a large consecutive sample of memory clinic patients. The consistency across the three tests applied lends credibility to our findings as does the observed pattern of association in all participants and most pronounced in less vulnerable participants. Notably, our findings are adjusted for key covariates, including age, gender, BMI, cognitive function, number of prescription drugs, and previous fall (yes/no). A further strength of our study is its population, which extends previous findings concerning individuals at risk of cognitive and functional decline assessed at a memory clinic setting. Our study also has several limitations. A key limitation is its cross-sectional design where interpretation is limited to associations rather than causality. Although we were able to adjust for important confounders, we may have missed others, such as physical activity, exercise, and skeletal muscle mass. However, physical activity is likely to be on the causal pathway between 25(OH)D and gait performance, which would have disqualified its inclusion in our analyses. Notably, exposure to sunlight, seasonal variations, body fat, dietary and supplement intake of vitamin D are reflected in the 25(OH)D status.

In summary and according to our findings, a higher 25(OH)D status seems to contribute to better normal and fast walking speed, as well as quicker TUG performance in seniors referred to a memory clinic. Notably, this positive association may be most pronounced in less vulnerable seniors, and a desirable threshold for optimal function in this subgroup may be >81 nmol/l. For the whole population assessed, also including vulnerable seniors, it seemed important for functional mobility to avoid a 25(OH)D status <39 nmol/l. Our data support measurement of 25(OH)D status in memory clinic patients, also for the observed positive association between higher 25(OH)D status and better cognitive performance.

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Disclosure Statement

The authors do not have any conflicts of interest to declare.

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